REMARKS

Amendments to the Claims

Claims 53, 69 and 72 have been amended to recite that the target antigen is a target antigen of a pathogenic organism. This amendment finds support at least in paragraphs [0015], [0081] and [0090] of the present specification and in original claim 16.

Claims 53, 69 and 72 also have been amended to recite primate antigen-presenting cells or their precursors, support for which can be found at least in paragraphs [0059] and [0150].

Claims 53, 69 and 72 also have been amended to exclude natural killer cells and natural killer T cells from the scope of what is encompassed by the term "antigen-presenting cells."

Claim 53 has been amended to delete the duplicated recitation "which have not been subjected to activating conditions."

Claims 56 and 70 have been amended to also exclude natural killer cells and natural killer T cells from the scope of what is encompassed by the term "heterogeneous population."

Newly added claim 80 recites that the pathogenic organism is a virus, support for which can be found at least in paragraph [0083].

Newly added claim 81 recites that the pathogenic organism is a retrovirus. Support for this amendment can be found at least in paragraphs [0083], in particular page 21, line 13 and paragraph [0087], in particular page 23, line 26.

Newly added claim 82 further recites that the retrovirus is an immunodeficiency virus. Support for this amendment can be found at least in paragraph [0083], in particular at page 21, line 10 and in paragraph [0091].

Newly added claim 83 further defines that the retrovirus is selected from human immunodeficiency virus and simian immunodeficiency virus, support for which can be found at least in paragraph [0083], in particular page 21, line 12 and in paragraph [0091].

Newly added claim 84 recites that the pathogenic organism is a hepatitis virus, which finds support at least in paragraph [0083], in particular page 21, lines 14-16 and in paragraph [0091], in particular page 25, line 4-5 and Table 13.

Newly added claim 85 further recites that the hepatitis virus is a hepatitis C virus, support for which can be found at least in paragraph [0083], in particular page 21, line 16 and in paragraph [0091], in particular page 25 lines 4-5 and Table 13.

Newly added claim 86 repeats recitation of claim 53 and further provides that interleukin-12 (IL-12) is excluded from the scope of the claimed composition. Support of the exclusion of IL-12 from the composition may be found, *inter alia*, in the examples provided in the specification, which do not employ IL-12. In addition, the specification contemplates the optional inclusion (*i.e.* presence or absence) of an adjuvant (*e.g.*, a lymphokine) in the claimed compositions at paragraph [0144] and specifically refers to NEW GENERATION VACCINES (Levine *et al.*, Marcel Dekker, Inc. New York, Basel, Hong Kong) at paragraph [0143] as providing exemplary procedures for making immunogenic compositions and vaccines. This textbook is incorporated by reference in its entirety at paragraph [0181] of the instant specification and IL-12 is listed as an adjuvant in Table 1 of Chapter 8 of this textbook (*see*, page 417). Relevant pages of NEW GENERATION VACCINES are ***enclosed*** for ease of reference.

Newly added claim 87 is similar to claim 53 and directed to a vaccine composition, support for which can be found at least in paragraphs [0143].

Newly added claim 88, which is also similar to claim 53, recites that the antigen-presenting cells or their precursors are selected from the group consisting of whole blood, fresh blood and irradiated blood. Support for that amendment can be found at least in paragraph [0018] and in original claims 46 and 47.

For the foregoing reasons, applicant respectfully submits that the amendments made herein are fully supported by the specification and do not include new matter.

Objections

Applicant respectfully requests that the objection to the declaration be held in abeyance until a newly signed declaration arrives by mail from the inventor in Australia and can be submitted.

Claim 53 has been amended in the manner suggested by the examiner to delete the recitation "which have not been subjected to activating conditions".

Rejection of Claims Pursuant to 35 U.S.C. § 112, first paragraph

Claims 53-68 and 73-79 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled for a composition that modulates an immune response in a subject to a target antigen wherein the composition comprises antigen-presenting cell precursors, or packed red cells, natural killer cells, and natural killer T cells. Applicant respectfully traverses.

The claims have been amended to exclude natural killer cells and natural killer T cells from the scope of the term "antigen-presenting cells". However, applicant respectfully submits that packed red cells and antigen-presenting cell precursors were known in the art at the filing date of the present application to include antigen-presenting cells or cells which are capable of differentiating into antigen-presenting cells for effective presentation of antigen to T cells.

Packed red blood cells (PRBC), also called "packed cells," are a preparation of red blood cells used to correct low blood levels in anemic patients. However, as can be seen from the provided PubMed abstract by Mascaretti *et al.* (2002, *Transfus Apher Sci*, **26**(3): 1672-1674), there is a significant white blood cell population in PRBC preparations, containing various lymphocyte subsets. Applicant respectfully asserts that the white blood cells in PRBC preparations would have the same antigen-presenting function as white blood cells in other blood preparations including peripheral blood mononuclear cells (PBMC). As such, it is not the red blood cells in the PRBC preparations that are contemplated for antigen presentation. Rather, it is the white blood cell population in PRBC that is considered useful for contacting with antigen to make antigen-pulsed antigen-presenting cells in accordance with the present invention.

Applicant also respectfully submits that the Examiner's assertion that the use of antigen-presenting cell precursors as antigen-presenting cells is highly unpredictable is incorrect. In this regard, it was well known at the filing date of the present application that dendritic cell/macrophage precursors capture endogenous antigens for MHC class I presentation (see, for example, Mitchell et al., 1998, *Eur. J. Immunol.* 28: 1923-1933, a copy of which is provided) and can present the antigen to T cells after maturing in the periphery (see, for example, Steinman, R. 1991, *Annu. Rev. Immunol.* 9: 271-296, a copy of which is also provided). Accordingly, these precursors are suitable for taking up antigen and for maturing *in vivo* when administered to a patient for effective modulation of T cells in the patient. The present specification further teaches how to obtain specific antigen-presenting cells precursors, including macrophage precursors (*see* paragraph [0106]) and dendritic cell precursors (*see* paragraph [0108] and [0109]) and it is submitted that in view of the knowledge that existed in the art and the guidance provided in the specification, a skilled artisan would be able to make suitable preparations of antigen-presenting cell precursors for contacting with antigen and for subsequent administration to patients for stimulating an immune response to a target antigen, without undue experimentation.

Rejection of claims pursuant to 35 USC § 102

Claims 53-62, 64-68 and 73-78 are rejected under 35 U.S.C. § 102 as allegedly anticipated by U.S. Patent No. 6,080,399 (the '399 patent). Applicant respectfully submits that the '399 patent is inapplicable to the amended claims.

Whatever the '399 patent teaches about admixing antigen with PBMC, irradiating the antigen pulsed PBMC and injecting the irradiated cells back into an animal or patient (*see* column 7, lines 40-47), it does not teach or suggest the compositions of the claims as presently amended. Applicant submits that it significant that in the '399 disclosure the injection of cells are co-administered with IL-12, which helps to stimulate the immune system to promote an anti-neoplastic or anti-disease response in the animal or patient (*see*, for example, column 5, lines 30-35 and 48-51; and column 7, lines 47-50 and 58-63). The '399 patent further highlights the importance of co-administering IL-12 with the peptide pulsed PBMC in the examples and in particular, please draw the Examiner's attention to Example 1 at column 33, lines 7-15 and 22 to 27. In fact, when peptide pulsed, mouse PBMC were used in the absence of IL-12, the cells did not elicit specific CTL activity (*see* column 33, lines 25-27 and column 34, lines 46-54 and Figure 5). The claims as amended distinguish over the disclosure of the '399 patent.

Specifically, the amended claims are drawn to a composition for modulating a subject's immune response to a target antigen of a pathogenic organism, wherein the composition comprises, *inter alia,* uncultured, non-activated primate antigen-presenting cells or their precursors, which have been contacted with an antigen corresponding to the target antigen. Applicant has discovered that these antigen-pulsed antigen-presenting cells are strong modulators of immune responses in primates and are especially useful for inducing high levels of CD4+ and CD8+ T cell responses against pathogenic organisms such as hepatitis C virus (HCV) and immunodeficiency viruses (e.g., HIV and SIV) without co-administration of IL-12. This contrasts with the teachings of the '399 patent, where it was found that one needed to co-administer IL-12 in a mouse cancer model.

Applicant submits that there is a significant distinction between the compositions described in the '399 patent, which are used in a mouse cancer model, and the instant claims, which recite compositions for preventing or treating infectious disease. Thus, the cells used in the '399 patent are treated with putative cancer antigens that are largely modified self-antigens, and require the presence of IL-12 for generating an immune response. By contrast, the instant claims recite cells that are treated with target antigens from one or more pathogenic organisms, which are non-self antigens, and where the IL-12 is neither necessary

nor present. Applicant respectfully directs the Examiner's attention to Example 2 and Figures 9 and 10 of the instance specification, , which show that SHIV or HCV peptide-pulsed whole blood produce high levels of antigen-specific $CD4^+$ and $CD8^+$ T cells in the absence of co-administering IL-12 (*see*, for instance, Example 2 and Figures 9 and 10 of the instance specification).

From the foregoing, it is clear that the '399 patent neither teaches nor suggests compositions comprising uncultured, non-activated primate antigen-presenting cells pulsed with antigen but lacking IL-12, for stimulating strong CTL and Th1 helper T cell responses in a primate against a target antigen of a pathogenic organism. Accordingly, the Examiner is respectfully urged to reconsider and withdraw the anticipation rejection under 35 USC § 102.

Rejection of claims pursuant to 35 USC § 103(a)

Claims 53-68 and 73-79 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,080,399 in view of Jager *et al.*, 2000. Jager is relied upon as a secondary reference and particularly discloses vaccination protocols which include MHC class II binding peptides. Jager, however, fails to cure the deficiencies of the '399 patent discussed above. In view of the foregoing, a *prima facie* case of obviousness has not been presented.

The Examiner is respectfully urged, therefore, to reconsider and withdraw the obviousness rejection under 35 USC § 103(a).

SUMMARY

Applicant respectfully submits that every rejection of the pending claims has been overcome and that each of claims 53-67 and 73-88 is in condition for allowance.

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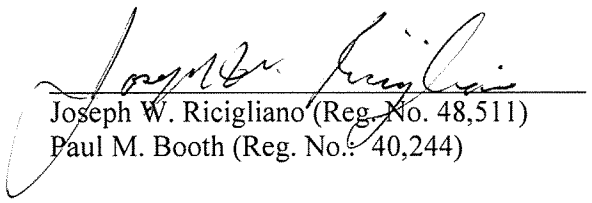
Respectfully submitted,



Joseph W. Ricigliano (Reg. No. 48,511)
Paul M. Booth (Reg. No. 40,244)

Attorneys for Applicant

Perkins Coie LLP
607 14th St., NW
Suite 800
Washington, DC 20005
Telephone: 202.628 6600
Facsimile: 202.434.1690

CUSTOMER NO: 91106